# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 141 | (Conteras$.in.)OR(Callewaert$.in. )OR(Vervecken$in. )OR(Kaigorodov$.in.) | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | AND | ON | 2006/07/20 15:03 |
| L2 | 11 | L1 AND glycosylation | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | AND | ON | 2006/07/20 15:04 |
| L3 | 8 | L1 AND mannose | US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB | AND | ON | 2006/07/20 15:04 |

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| NEWS 4 | APR 04 | STN AnaVist $500 visualization usage credit offered |
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| NEWS 6 | MAY 11 | KOREAPAT updates resume |
| NEWS 7 | MAY 19 | Derwent World Patents Index to be reloaded and enhanced |
| NEWS 8 | MAY 30 | IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2 |
| NEWS 9 | MAY 30 | The F-Term thesaurus is now available in CA/CAplus |
| NEWS 10 | JUN 02 | The first reclassification of IPC codes now complete in INPADOC |
| NEWS 11 | JUN 26 | TULSA/TULSA2 reloaded and enhanced with new search and and display fields |
| NEWS 12 | JUN 28 | Price changes in full-text patent databases EPFULL and PCTFULL |
| NEWS 13 | JUl 11 | CHEMSAFE reloaded and enhanced |
| NEWS 14 | JUl 14 | FSTA enhanced with Japanese patents |
| NEWS 15 | JUl 19 | Coverage of Research Disclosure reinstated in DWPI |

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |
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FILE 'HOME' ENTERED AT 14:39:52 ON 20 JUL 2006

=> File CAPLUS

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| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'CAPLUS' ENTERED AT 14:40:16 ON 20 JUL 2006

FILE COVERS 1907 - 20 Jul 2006 VOL 145 ISS 4
FILE LAST UPDATED: 19 Jul 2006 (20060719/ED)



```
=> s glycoprotein
         97485 GLYCOPROTEIN
        106943 GLYCOPROTEINS
L1      150064 GLYCOPROTEIN
                (GLYCOPROTEIN OR GLYCOPROTEINS)

=> s L1 AND yeast AND human
        195608 YEAST
         33377 YEASTS
        203764 YEAST
                (YEAST OR YEASTS)
       1623485 HUMAN
        337848 HUMANS
       1789583 HUMAN
                (HUMAN OR HUMANS)
L2         881 L1 AND YEAST AND HUMAN

=> s GnT1
L3          14 GNT1

=> s acetylglucosaminyltransferase
          1624 ACETYLGLUCOSAMINYLTRANSFERASE
           179 ACETYLGLUCOSAMINYLTRANSFERASES
L4        1667 ACETYLGLUCOSAMINYLTRANSFERASE
                (ACETYLGLUCOSAMINYLTRANSFERASE OR ACETYLGLUCOSAMINYLTRANSFERAS
                ES)

=> s L2 AND L4
L5          27 L2 AND L4

=> d 1-27 ti, so L5

L5   ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Transgenic fungi expressing mannosidase, GnTI, GnTII, and/or GalT genes
     for preparation of proteins with mammalian N-glycan structure
SO   PCT Int. Appl., 84 pp.
     CODEN: PIXXD2

L5   ANSWER 2 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Genetically engineered yeast for production of human
```

-like glycoproteins with terminal galactose residues
SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2

L5 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Alg14 Recruits Alg13 to the Cytoplasmic Face of the Endoplasmic Reticulum to Form a Novel Bipartite UDP-N-acetylglucosamine Transferase Required for the Second Step of N-Linked Glycosylation
SO Journal of Biological Chemistry (2005), 280(43), 36254-36262
CODEN: JBCHA3; ISSN: 0021-9258

L5 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI N-acetylglucosamintransferase III expression in genetically modified lower eukaryotes
SO U.S. Pat. Appl. Publ., 163 pp., Cont.-in-part of U.S. Ser. No. 371,877.
CODEN: USXXCO

L5 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI The curcuminoids- and anthocyanins-responsive genes in human adipocytes and their use in screenings of anti-obesity and anti-diabetes drugs
SO Jpn. Kokai Tokkyo Koho, 85 pp.
CODEN: JKXXAF

L5 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI N-acetylglucosaminyltransferase III and other N-glycan-processing enzymes expressed in lower eukaryotes for the biosynthesis of human-like oligosaccharide structures in glycoproteins
SO PCT Int. Appl., 193 pp.
CODEN: PIXXD2

L5 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Engineering of an artificial glycosylation pathway blocked in core oligosaccharide assembly in the yeast Pichia pastoris: Production of complex humanized glycoproteins with terminal galactose
SO Glycobiology (2004), 14(9), 757-766
CODEN: GLYCE3; ISSN: 0959-6658

L5 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Methods for glycan remodeling and glycoPEGylation of therapeutic proteins
SO U.S. Pat. Appl. Publ., 690 pp., Cont.-in-part of U.S. Ser. No. 360 ,779.
CODEN: USXXCO

L5 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Human tissue-specific housekeeping genes identified by expression profiling
SO PCT Int. Appl., 372 pp.
CODEN: PIXXD2

L5 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Erythropoietin glycosylation and the modification of protein structure and activity for therapeutic use
SO PCT Int. Appl., 1018 pp.
CODEN: PIXXD2

L5 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Glycan remodeling and glycoconjugation of granulocyte colony stimulating factor
SO U.S. Pat. Appl. Publ., 754 pp., Cont.-in-part of U.S. Ser. No. 360,779.
CODEN: USXXCO

L5 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Remodeling of protein-linked oligosaccharide moieties and the resulting glycoproteins and glycopeptides
SO U.S. Pat. Appl. Publ., 749 pp., Cont.-in-part of U.S. Ser. No. 360,779.
CODEN: USXXCO

L5 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Fusion proteins and methods of producing same
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2

L5 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Combinatorial DNA library of mammalian glycosylation enzyme genes used for producing modified n-glycans in lower eukaryotes
SO U.S. Pat. Appl. Publ., 97 pp., Cont.-in-part of U.S. Ser. No. 892,591.
CODEN: USXXCO

L5 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Production of glycoproteins with modified glycosylation in Pichia pastoris
SO PCT Int. Appl., 172 pp.
CODEN: PIXXD2

L5 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Finding of O-mannosyl glycan in mammals and congenital muscular dystrophies due to glycosylation defects
SO Yakugaku Zasshi (2003), 123(10), 825-835
CODEN: YKKZAJ; ISSN: 0031-6903

L5 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Methods for production of recombinant glycoproteins with mammalian-type carbohydrate structures and their use for production of immunoglobulins
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2

L5 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Use of combinatorial genetic libraries to humanize N-linked glycosylation in the yeast Pichia pastoris
SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(9), 5022-5027
CODEN: PNASA6; ISSN: 0027-8424

L5 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Methods for serial analysis of gene expression of renal dipeptidase in colorectal tumors and their use in diagnosis
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2

L5 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Modification of the N-glycosylation pathway of lower eukaryotes to a mammalian type
SO Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), BIOT-030 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69DSA4

L5 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
SO Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF

L5 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Sequence of human N-acetylglucosaminyltransferase and the uses in biosynthesis of mammalian O-mannosyl glycans
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2

L5 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Exploring the acceptor substrate recognition of the human β-galactoside α2,6-sialyltransferase
SO Journal of Biological Chemistry (2001), 276(24), 21608-21617
CODEN: JBCHA3; ISSN: 0021-9258

L5 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI UDP-N-acetylglucosamine:galactose-β1,3-N-acetylgalactosamine-α-R/(GlcNAc to GalNAc) β1,6-N- acetylglucosaminyltransferase C2GnT3 and its cDNA sequence from human thymus
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2

L5 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Production of human compatible high mannose-type sugar chains in Saccharomyces cerevisiae auxotrophic mutants with sugar chain biosynthesis-associated genes
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2

L5 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Engineering of intracellular sialylation pathways for sialylated glycoprotein production
SO PCT Int. Appl., 145 pp.
CODEN: PIXXD2

L5 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Expression and characterization of rat UDP-N-acetylglucosamine: α-3-D-mannoside β-1,2-N- acetylglucosaminyltransferase I in Saccharomyces cerevisiae
SO Glycobiology (1999), 9(1), 53-58
CODEN: GLYCE3; ISSN: 0959-6658

=> dup rem L5
PROCESSING COMPLETED FOR L5
L6 27 DUP REM L5 (0 DUPLICATES REMOVED)

=> d ti, so, ibib, abs 1,2,6,7,8,10-15,17,18,20,26 L5

L5 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Transgenic fungi expressing mannosidase, GnTI, GnTII, and/or GalT genes for preparation of proteins with mammalian N-glycan structure
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
ACCESSION NUMBER: 2006:240500 CAPLUS
DOCUMENT NUMBER: 144:287450
TITLE: Transgenic fungi expressing mannosidase, GnTI, GnTII, and/or GalT genes for preparation of proteins with mammalian N-glycan structure
INVENTOR(S): Joergensen, Christel Thea; Hjort, Carsten
PATENT ASSIGNEE(S): Novozymes A/S, Den.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006026992 | A1 | 20060316 | WO 2005-DK569 | 20050907 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DK 2004-1346 A 20040907

AB The present invention relates to methods for altering the structure of N-glycans in fungal cells and to fungal cells having an altered N-glycan structure. The fungi express one or more of the genes encoding α-1,2-mannosidase, 1,3-1,6-α-manosidase (mannosidase II, E.C. 3.2.1.114), α-1,3-mannosylglycoprotein 2-β-N-acetylglucosaminyltransferase (GnT1, E.C. 2.4.1.101), α-1,6-mannosylglycoprotein 2-β-N-acetylglucosaminyltransferase (GnTII, E.C. 2.4.1.143), and 1,4-galactosyltransferase (GalT, E.C. 2.4.1.38). Transgenic fungi expressing one or more of these genes may be used in production of mammalian proteins, e.g., human monoclonal antibodies. Thus, Aspergillus oryzae expressing A. nidulans mannosidase IC gene produced heterologous protein with Man5GlcNAc2 N-glycan structure.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

TI Genetically engineered yeast for production of human -like glycoproteins with terminal galactose residues

SO PCT Int. Appl., 120 pp.
CODEN: PIXXD2

ACCESSION NUMBER: 2005:1154698 CAPLUS
DOCUMENT NUMBER: 143:433718
TITLE: Genetically engineered yeast for production of human-like glycoproteins with terminal galactose residues
INVENTOR(S): Davidson, Robert; Gerngross, Tillman; Wildt, Stefan; Choi, Byung-Kwon; Nett, Juergen; Bobrowicz, Piotr; Hamilton, Stephen
PATENT ASSIGNEE(S): Glycofi, Inc., USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005100584 | A2 | 20051027 | WO 2005-IB51249 | 20050415 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,

SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-562424P P 20040415

AB The invention provides a lower eukaryotic host cell producing human-like glycoproteins characterized as having a terminal β-galactose residue and essentially lacking fucose and sialic acid residues. The invention also provides methods and compns., including genetic vectors, for catalyzing the transfer of a galactose residue from UDP-galactose onto an acceptor substrate in a recombinant lower eukaryotic host cell. In addition to a UDP-Gal:βGlcNAc β-1,4-galactosyltransferase, expression of UDP-galactose transporter(s), a UDP-specific diphosphatase, and UDP-galactose-4-epimerase, galactokinase, or galactose-1-phosphate uridyltransferase activities allow transfer of galactose residues onto preferred acceptor substrates for use as therapeutic glycoproteins. The invention claims polypeptide sequences for gene galE UDP-galactose C4 epimerase enzyme and conserved motifs. Methods of the invention can be applied to therapeutic glycoproteins such as erythropoietin, cytokines, blood coagulation factors, Igs, growth factors, or plasminogen. The examples provide maps of integrating plasmid vectors encoding human GalTI, S. pombe gene galE epimerase, and D. melanogaster gene UGT UDP-galactose transporter. The secreted kringle 3 (K3) domain of plasminogen was the reporter protein for glycosylation in transformed Pichia pastoris strains. N-linked glycans obtained from K3 were analyzed by MALDI-TOF mass spectrometry. A P. pastoris strain with och1 and alg3 gene deletions, active fusion constructs of mouse mannosidase IB and human GnTI, the Kluyveromyces lactis UDP-GlcNAc transporter gene, and a human GalTI gene leader fusion construct had approx. 10-20% of GlcNAc2Man3GlcNAc2 N-glycans on K3 converted to GalGlcNAc2Man3GlcNAc2 and 1-2% to Gal2GlcNAc2Man3GlcNAc2. When a strain with the same genotype was also transformed with the Saccharomyces cerevisiae epimerase gene GAL10 under control of the PMAI promoter, about 2/3 of the N-glycans released from K3 contained an addnl. hexose residue (HexGlcNAcMan5GlcNAc2) that could be removed by soluble β-1,4-galactosidase.

L5 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

TI N-acetylglucosaminyltransferase III and other N-glycan-processing enzymes expressed in lower eukaryotes for the biosynthesis of human-like oligosaccharide structures in glycoproteins

SO PCT Int. Appl., 193 pp.
CODEN: PIXXD2

ACCESSION NUMBER: 2004:720587 CAPLUS
DOCUMENT NUMBER: 141:237748
TITLE: N-acetylglucosaminyltransferase III and other N-glycan-processing enzymes expressed in lower eukaryotes for the biosynthesis of human -like oligosaccharide structures in glycoproteins
INVENTOR(S): Bobrowicz, Piotr; Hamilton, Stephen R.; Gerngross, Tillman U.; Wildt, Stefan; Choi, Byung-Kwon; Nett, Juergen Hermann; Davidson, Robert C.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004074458 | A2 | 20040902 | WO 2004-US5128 | 20040220 |
| WO 2004074458 | A3 | 20041229 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004018590 | A1 | 20040129 | US 2003-371877 | 20030220 |
| US 2005208617 | A1 | 20050922 | US 2003-680963 | 20031007 |
| AU 2004213859 | A1 | 20040902 | AU 2004-213859 | 20040220 |
| CA 2516520 | AA | 20040902 | CA 2004-2516520 | 20040220 |
| EP 1599595 | A2 | 20051130 | EP 2004-713412 | 20040220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 2003-371877 | A | 20030220 |
| US 2003-680963 | A | 20031007 |
| US 2000-214358P | P | 20000628 |
| US 2000-215638P | P | 20000630 |
| US 2001-279997P | P | 20010330 |
| US 2001-892591 | A2 | 20010627 |
| US 2001-344169P | P | 20011227 |
| WO 2002-US41510 | A2 | 20021224 |
| WO 2004-US5128 | A | 20040220 |

AB The present invention relates to eukaryotic host cells having modified oligosaccharides which may be modified further by heterologous expression of a set of glycosyltransferases, sugar transporters, and mannosidases to become host-strains for the production of mammalian, e.g., human therapeutic glycoproteins. The process provides an engineered host cell such as Pichia pastoris which can be used to express and target any desirable gene(s) involved in glycosylation. Host cells with modified lipid-linked oligosaccharides are created or selected. N-glycans made in the engineered host cells exhibit N-acetylglucosaminyltransferase III (GnTIII) activity, which produce bisected N-glycan structures and may be modified further by heterologous expression of one or more enzymes, e.g., glycosyltransferases, sugar transporters and mannosidases, to yield human-like glycoproteins. For the production of therapeutic proteins, this method may be adapted to engineer cell lines in which any desired glycosylation structure may be obtained.

L5 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Engineering of an artificial glycosylation pathway blocked in core oligosaccharide assembly in the yeast Pichia pastoris: Production of complex humanized glycoproteins with terminal galactose
SO Glycobiology (2004), 14(9), 757-766
CODEN: GLYCE3; ISSN: 0959-6658
ACCESSION NUMBER: 2004:702495 CAPLUS
DOCUMENT NUMBER: 141:391680
TITLE: Engineering of an artificial glycosylation pathway blocked in core oligosaccharide assembly in the yeast Pichia pastoris: Production of complex humanized glycoproteins with terminal galactose
AUTHOR(S): Bobrowicz, Piotr; Davidson, Robert C.; Li, Huijuan; Potgieter, Thomas I.; Nett, Juergen H.; Hamilton,

Stephen R.; Stadheim, Terrance A.; Miele, Robert G.; Bobrowicz, Beata; Mitchell, Teresa; Rausch, Sebastian; Renfer, Eduard; Wildt, Stefan

CORPORATE SOURCE: GlycoFi, Inc., Lebanon, NH, 03766, USA

SOURCE: Glycobiology (2004), 14(9), 757-766
CODEN: GLYCE3; ISSN: 0959-6658

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A significant percentage of eukaryotic proteins contain post-translational modifications, including glycosylation, which are required for biol. function. However, the understanding of the structure-function relationships of N-glycans has lagged significantly due to the microheterogeneity of glycosylation in mammalian produced proteins. Recently we reported on the cellular engineering of yeast to replicate human N-glycosylation for the production of glycoproteins. Here we report the engineering of an artificial glycosylation pathway in Pichia pastoris blocked in dolichol oligosaccharide assembly. The PpALG3 gene encoding Dol-P-Man:-Man5GlcNAc2-PP-Dol mannosyltransferase was deleted in a strain that was previously engineered to produce hybrid GlcNAcMan5GlcNAc2 human N-glycans. Employing this approach, combined with the use of combinatorial genetic libraries, we engineered P. pastoris strains that synthesize complex GlcNAc2Man3GlcNAc2 N-glycans with striking homogeneity. Furthermore, through expression of a Golgi-localized fusion protein comprising UDP-glucose 4-epimerase and β-1,4-galactosyl transferase activities we demonstrate that this structure is a substrate for highly efficient in vivo galactose addition Taken together, these data demonstrate that the artificial in vivo glyco-engineering of yeast represents a major advance in the production of glycoproteins and will emerge as a practical tool to systematically elucidate the structure-function relationship of N-glycans.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

TI Methods for glycan remodeling and glycoPEGylation of therapeutic proteins

SO U.S. Pat. Appl. Publ., 690 pp., Cont.-in-part of U.S. Ser. No. 360 ,779.
CODEN: USXXCO

ACCESSION NUMBER: 2004:589223 CAPLUS

DOCUMENT NUMBER: 141:122414

TITLE: Methods for glycan remodeling and glycoPEGylation of therapeutic proteins

INVENTOR(S): Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi

PATENT ASSIGNEE(S): Neose Technologies, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 690 pp., Cont.-in-part of U.S. Ser. No. 360 ,779.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004142856 | A1 | 20040722 | US 2003-410913 | 20030409 |
| WO 2003031464 | A2 | 20030417 | WO 2002-US32263 | 20021009 |
| WO 2003031464 | A3 | 20060302 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| US 2004137557 | A1 | 20040715 | US 2002-287994 | | 20021105 |
| AU 2004236174 | A1 | 20041118 | AU 2004-236174 | | 20040409 |
| CA 2522345 | AA | 20041118 | CA 2004-2522345 | | 20040409 |
| WO 2004099231 | A2 | 20041118 | WO 2004-US11494 | | 20040409 |
| WO 2004099231 | A3 | 20060316 | | | |

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| EP 1615945 | A2 | 20060118 | EP 2004-750118 | | 20040409 |

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| BR 2004009277 | A | 20060321 | BR 2004-9277 | | 20040409 |

PRIORITY APPLN. INFO.:

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| US 2001-328523P | P | 20011010 |
| US 2001-344692P | P | 20011019 |
| US 2001-334233P | P | 20011128 |
| US 2001-334301P | P | 20011128 |
| US 2002-387292P | P | 20020607 |
| US 2002-391777P | P | 20020625 |
| US 2002-396594P | P | 20020717 |
| US 2002-404249P | P | 20020816 |
| US 2002-407527P | P | 20020828 |
| WO 2002-US32263 | A1 | 20021009 |
| US 2002-287994 | A2 | 20021105 |
| US 2003-360770 | A2 | 20030106 |
| US 2003-438582P | P | 20030106 |
| US 2003-360779 | A2 | 20030219 |
| US 2003-448381P | P | 20030219 |
| US 2003-410897 | A | 20030409 |
| US 2003-410913 | A | 20030409 |
| US 2003-410930 | A | 20030409 |
| US 2003-410945 | A | 20030409 |
| US 2003-410962 | A | 20030409 |
| US 2003-410980 | A | 20030409 |
| US 2003-410997 | A | 20030409 |
| US 2003-411012 | A | 20030409 |
| US 2003-411026 | A | 20030409 |
| US 2003-411037 | A | 20030409 |
| US 2003-411043 | A | 20030409 |
| US 2003-411044 | A | 20030409 |
| US 2003-411049 | A | 20030409 |
| WO 2004-US11494 | A | 20040409 |

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. Thus, polyethylene glycols were conjugated to CMP or UDP nucleosides for use in modifying recombinant therapeutic proteins.

L5 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Erythropoietin glycosylation and the modification of protein structure and

activity for therapeutic use
SO PCT Int. Appl., 1018 pp.
CODEN: PIXXD2

ACCESSION NUMBER: 2004:333839 CAPLUS
DOCUMENT NUMBER: 140:352406
TITLE: Erythropoietin glycosylation and the modification of protein structure and activity for therapeutic use
INVENTOR(S): De Frees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi
PATENT ASSIGNEE(S): Neose Technologies, Inc., USA
SOURCE: PCT Int. Appl., 1018 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004033651 | A2 | 20040422 | WO 2003-US31974 | 20031008 |
| WO 2004033651 | A3 | 20060330 | | |
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| WO 2003031464 | A2 | 20030417 | WO 2002-US32263 | 20021009 |
| WO 2003031464 | A3 | 20060302 | | |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004137557 | A1 | 20040715 | US 2002-287994 | 20021105 |
| CA 2501832 | AA | 20040422 | CA 2003-2501832 | 20031008 |
| AU 2003287035 | A1 | 20040504 | AU 2003-287035 | 20031008 |
| BR 2003015178 | A | 20050816 | BR 2003-15178 | 20031008 |
| EP 1581622 | A2 | 20051005 | EP 2003-777555 | 20031008 |
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| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| WO 2002-US32263 | A | 20021009 |
| US 2002-287994 | A | 20021105 |
| US 2003-360770 | A | 20030106 |
| US 2003-360779 | A | 20030219 |
| US 2003-410945 | A | 20030409 |
| US 2001-328523P | P | 20011010 |
| US 2001-344692P | P | 20011019 |
| US 2001-334233P | P | 20011128 |
| US 2001-334301P | P | 20011128 |
| US 2002-387292P | P | 20020607 |
| US 2002-391777P | P | 20020625 |
| US 2002-396594P | P | 20020717 |
| US 2002-404249P | P | 20020816 |

US 2002-407527P P 20020828
WO 2003-US31974 W 20031008

AB The invention includes methods and compns. for remodeling a peptide mol., including the addition or deletion of one or more glycosyl groups to a peptide, and/or the addition of a modifying group to a peptide. Methods of modifying the structure and properties of erythropoietin by introduction of glycosidation are described. The method uses substitution variants of erythropoietin to introduce sites that can be glycosylated enzymically. The primary glycosylation may then be used to add further sugar residues. The glycosidation, which may include the introduction of N-acetylglucose, N-acetylgalactose, and sialic acid and mannosyl and fucosyl oligosaccharides. The carbohydrate moiety may in turn be modified by PEGylation. A biantennary glycosidated derivative of Epogen had 146% of the activity of the unmodified protein. The glycosylated proteins had longer serum half-lives than the unmodified protein and showed longer term effects on blood Hb levels.

L5 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Glycan remodeling and glycoconjugation of granulocyte colony stimulating factor
SO U.S. Pat. Appl. Publ., 754 pp., Cont.-in-part of U.S. Ser. No. 360,779. CODEN: USXXCO

ACCESSION NUMBER: 2004:331821 CAPLUS
DOCUMENT NUMBER: 140:353209
TITLE: Glycan remodeling and glycoconjugation of granulocyte colony stimulating factor
INVENTOR(S): Defrees, Shawn; Zopf, David; Bayer, Robert; Bowe, Caryn; Hakes, David; Chen, Xi
PATENT ASSIGNEE(S): Neose Technologies, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 754 pp., Cont.-in-part of U.S. Ser. No. 360,779.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004077836 | A1 | 20040422 | US 2003-410962 | 20030409 |
| WO 2003031464 | A2 | 20030417 | WO 2002-US32263 | 20021009 |
| WO 2003031464 | A3 | 20060302 | | |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| US 2004137557 | A1 | 20040715 | US 2002-287994 | 20021105 |
| AU 2004236174 | A1 | 20041118 | AU 2004-236174 | 20040409 |
| CA 2522345 | AA | 20041118 | CA 2004-2522345 | 20040409 |
| WO 2004099231 | A2 | 20041118 | WO 2004-US11494 | 20040409 |
| WO 2004099231 | A3 | 20060316 | | |

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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| EP 1615945 | A2 | 20060118 | EP 2004-750118 | 20040409 |
| BR 2004009277 | A | 20060321 | BR 2004-9277 | 20040409 |

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PRIORITY APPLN. INFO.:

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| US 2001-344692P | P | 20011019 |
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| US 2002-387292P | P | 20020607 |
| US 2002-391777P | P | 20020625 |
| US 2002-396594P | P | 20020717 |
| US 2002-404249P | P | 20020816 |
| US 2002-407527P | P | 20020828 |
| WO 2002-US32263 | A1 | 20021009 |
| US 2002-287994 | A2 | 20021105 |
| US 2003-360770 | A2 | 20030106 |
| US 2003-360779 | A2 | 20030219 |
| US 2003-410897 | A | 20030409 |
| US 2003-410913 | A | 20030409 |
| US 2003-410930 | A | 20030409 |
| US 2003-410945 | A | 20030409 |
| US 2003-410962 | A | 20030409 |
| US 2003-410980 | A | 20030409 |
| US 2003-410997 | A | 20030409 |
| US 2003-411012 | A | 20030409 |
| US 2003-411026 | A | 20030409 |
| US 2003-411037 | A | 20030409 |
| US 2003-411043 | A | 20030409 |
| US 2003-411044 | A | 20030409 |
| US 2003-411049 | A | 20030409 |
| WO 2004-US11494 | A | 20040409 |

AB The invention includes a multitude of methods of remodeling a peptide to have a specific glycan structure attached to the peptide. The methods comprise cell-free in vitro addition and/or deletion of sugars to or from a peptide mol. in such a manner as to provide a glycopeptide mol. having a specific customized or desired glycosylation pattern, wherein the glycopeptide is produced at an industrial scale and is suitable for therapeutic use in a mammal. The modified sugar that has been added to the peptide is generated via an enzymic reaction, because enzyme-based addition of conjugate mols. to peptides has the advantage of regioselectivity and stereoselectivity. Thus, a granulocyte colony stimulating factor (G-CSF) peptide that is expressed in a mammalian cell system is trimmed back using a sialidase. The residues thus exposed are modified by the addition of a sialic acid-poly(ethylene glycol) moiety, using an appropriate donor therefor and ST3Gal1. Mammalian cell expressed G-CSF is contacted with a sialic acid donor that is modified with levulinic acid, adding a reactive ketone to the sialic acid donor. After addition to a glycosyl residue on the glycan on the peptide, the ketone is derivatized with a moiety such as hydrazine- or amino-PEG. Analogous schemes are provided for G-CSF expressed in an insect or bacterial cell.

L5 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

TI Remodeling of protein-linked oligosaccharide moieties and the resulting glycoproteins and glycopeptides

SO U.S. Pat. Appl. Publ., 749 pp., Cont.-in-part of U.S. Ser. No. 360,779. CODEN: USXXCO

ACCESSION NUMBER: 2004:269906 CAPLUS

DOCUMENT NUMBER: 140:300039

TITLE: Remodeling of protein-linked oligosaccharide moieties and the resulting glycoproteins and glycopeptides

INVENTOR(S): Defree, Shawn; Zopf, David; Bayer, Robert; Hakes, David; Chen, Xi

PATENT ASSIGNEE(S): Neose Technologies Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 749 pp., Cont.-in-part of U.S. Ser. No. 360,779.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004063911 | A1 | 20040401 | US 2003-411026 | 20030409 |
| WO 2003031464 | A2 | 20030417 | WO 2002-US32263 | 20021009 |
| WO 2003031464 | A3 | 20060302 | | |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004137557 | A1 | 20040715 | US 2002-287994 | 20021105 |
| AU 2004236174 | A1 | 20041118 | AU 2004-236174 | 20040409 |
| CA 2522345 | AA | 20041118 | CA 2004-2522345 | 20040409 |
| WO 2004099231 | A2 | 20041118 | WO 2004-US11494 | 20040409 |
| WO 2004099231 | A3 | 20060316 | | |
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| EP 1615945 | A2 | 20060118 | EP 2004-750118 | 20040409 |
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| BR 2004009277 | A | 20060321 | BR 2004-9277 | 20040409 |

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| US 2001-328523P | P | 20011010 |
| US 2001-344692P | P | 20011019 |
| US 2001-334233P | P | 20011128 |
| US 2001-334301P | P | 20011128 |
| US 2002-387292P | P | 20020607 |
| US 2002-391777P | P | 20020625 |
| US 2002-396594P | P | 20020717 |
| US 2002-404249P | P | 20020816 |
| US 2002-407527P | P | 20020828 |
| WO 2002-US32263 | A1 | 20021009 |
| US 2002-287994 | A2 | 20021105 |
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| US 2003-410897 | A | 20030409 |

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| US 2003-410913 | A | 20030409 |
| US 2003-410930 | A | 20030409 |
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| US 2003-410997 | A | 20030409 |
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| US 2003-411037 | A | 20030409 |
| US 2003-411043 | A | 20030409 |
| US 2003-411044 | A | 20030409 |
| US 2003-411049 | A | 20030409 |
| WO 2004-US11494 | A | 20040409 |

AB The invention includes a multitude of methods of remodeling a peptide to have a specific glycan structure attached to the peptide. The methods comprise cell-free in vitro addition and/or deletion of sugars to or from a peptide mol. in such a manner as to provide a glycopeptide mol. having a specific customized or desired glycosylation pattern, wherein the glycopeptide is produced at an industrial scale. The modified sugar that has been added to the peptide is generated via an enzymic reaction, because enzyme-based addition of conjugate mols. to peptides has the advantage of regioselectivity and stereoselectivity. A key feature of the invention is to take a peptide produced by any cell type and generate a core glycan structure on the peptide, following which the glycan structure is then remodeled in vitro to generate a glycopeptide having a glycosylation pattern suitable for therapeutic use in a mammal.

L5 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Fusion proteins and methods of producing same
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2

ACCESSION NUMBER: 2004:143251 CAPLUS
DOCUMENT NUMBER: 140:213579
TITLE: Fusion proteins and methods of producing same
INVENTOR(S): Holgersson, Jan; Liu, Jining; Gustafsson, Anki
PATENT ASSIGNEE(S): Absorber Ab, Swed.; Recopharma Ab
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004015057 | A2 | 20040219 | WO 2003-IB3881 | 20030811 |
| WO 2004015057 | C2 | 20040729 | | |
| WO 2004015057 | A3 | 20050120 | | |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2495743 | AA | 20040219 | CA 2003-2495743 | 20030811 |
| AU 2003263411 | A1 | 20040225 | AU 2003-263411 | 20030811 |
| US 2004137580 | A1 | 20040715 | US 2003-638820 | 20030811 |
| EP 1534748 | A2 | 20050601 | EP 2003-784433 | 20030811 |
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| JP 2005535699 | T2 | 20051124 | JP 2004-527246 | | 20030811 |
| PRIORITY APPLN. INFO.: | | | US 2002-402211P | P | 20020809 |
| | | | WO 2003-IB3881 | W | 20030811 |

AB The invention provides mucin-Ig fusion proteins (αGal fusion proteins) containing multiple αGal epitopes that are useful as an absorber for anti-αGal antibodies (i.e. for their removal from blood or plasma prior to a xenotransplantation.). Methods of producing the fusion proteins are also provided. The invention is based in part in the discovery that the carbohydrate epitope Galα1,3Gal (αGal) can be specifically expressed at high d. and by different core saccharide chains on mucin-type protein backbones. More particularly, the invention is based upon the surprising discovery that expression of αGal epitopes of mucin-type protein backbones is dependent upon the cell line expressing the polypeptide. Moreover, the glycan repertoire of the mucin can be modified by co-expression of exogenous α1,3 galactosyltransferase and a core 2 branching enzyme. This modification results in a higher d. of αGal epitopes and an increased binding or removal (i.e., absorption) of anti-αGal antibodies as compared to free saccharides, αGal determinants linked to solid phase, or cells transfected with α1,3 galactosyltransferase alone. Transient transfection of a PSGL-1/mIgG2b fusion protein and porcine α1,3galactosyltransferase (α1,3GalT) in COS cells results in a dimeric fusion protein heavily substituted with αGal epitopes. The fusion protein has approx. terminal αGal epitopes per dimer and a xenoreactive natural antibodies (XNAb) adsorption efficiency 20 times higher (on a carbohydrate molar basis) than pig thyroglobulin immobilized on agarose beads, and 5,000 and 30,000 times higher than Galα1,3Gal-conjugated agarose and macroporous glass beads, resp. To investigate the importance of the host cell for αGal epitope d. on, and anti-pig antibody adsorption efficacy of, PSGL-1/mIgG2b, the protein, together with the porcine α1,3GalT, was stably expressed in CHO, COS and 293T cells. The level of αGal substitution on PSGL-1/mIgG2b and its anti-pig antibody adsorption capacity were dependent on the host cell. PSGL-1/mIgG2b made in COS cells exhibited a 5.3-fold increase in the relative O.D. (GSA-reactivity/anti-mouse IgG reactivity) compared to PSGL-1/mIgG2b made in COS without the α1,3GalT. Similarly, PSGL-1/mIgG2b made in 293T cells exhibited a 3.1-fold increase in the relative O.D. In contrast, PSGL-1/mIgG2b made in CHO cells exhibited only a 1.8-fold increase. The anti-pig antibody adsorption efficacy of PSGL-1/mIgG2b made in different host cells correlated to its degree of αGal substitution.

L5 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

TI Combinatorial DNA library of mammalian glycosylation enzyme genes used for producing modified n-glycans in lower eukaryotes

SO U.S. Pat. Appl. Publ., 97 pp., Cont.-in-part of U.S. Ser. No. 892,591. CODEN: USXXCO

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| ACCESSION NUMBER: | 2004:80241 CAPLUS |
| DOCUMENT NUMBER: | 140:158561 |
| TITLE: | Combinatorial DNA library of mammalian glycosylation enzyme genes used for producing modified n-glycans in lower eukaryotes |
| INVENTOR(S): | Gerngross, Tillman U.; Wildt, Stefan; Choi, Byung-Kwon; Nett, Juergen Hermann; Bobrowicz, Piotr; Hamilton, Stephen R.; Davidson, Robert C. |
| PATENT ASSIGNEE(S): | USA |
| SOURCE: | U.S. Pat. Appl. Publ., 97 pp., Cont.-in-part of U.S. Ser. No. 892,591. CODEN: USXXCO |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 20 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US 2004018590 | A1 | 20040129 | US 2003-371877 | 20030220 |
| US 2002137134 | A1 | 20020926 | US 2001-892591 | 20010627 |
| US 7029872 | B2 | 20060418 | | |
| EP 1522590 | A1 | 20050413 | EP 2004-25648 | 20010627 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| US 2004230042 | A1 | 20041118 | US 2003-616082 | 20030708 |
| US 2005208617 | A1 | 20050922 | US 2003-680963 | 20031007 |
| US 2004171826 | A1 | 20040902 | US 2003-695243 | 20031027 |
| AU 2004213859 | A1 | 20040902 | AU 2004-213859 | 20040220 |
| AU 2004213860 | A1 | 20040902 | AU 2004-213860 | 20040220 |
| AU 2004213861 | A1 | 20040902 | AU 2004-213861 | 20040220 |
| AU 2004213868 | A1 | 20040902 | AU 2004-213868 | 20040220 |
| AU 2004213869 | A1 | 20040902 | AU 2004-213869 | 20040220 |
| CA 2516440 | AA | 20040902 | CA 2004-2516440 | 20040220 |
| CA 2516520 | AA | 20040902 | CA 2004-2516520 | 20040220 |
| CA 2516527 | AA | 20040902 | CA 2004-2516527 | 20040220 |
| CA 2516544 | AA | 20040902 | CA 2004-2516544 | 20040220 |
| CA 2516550 | AA | 20040902 | CA 2004-2516550 | 20040220 |
| WO 2004074458 | A2 | 20040902 | WO 2004-US5128 | 20040220 |
| WO 2004074458 | A3 | 20041229 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| WO 2004074497 | A2 | 20040902 | WO 2004-US5131 | 20040220 |
| WO 2004074497 | A3 | 20041202 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| WO 2004074498 | A2 | 20040902 | WO 2004-US5132 | 20040220 |
| WO 2004074498 | A3 | 20050623 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| WO 2004074461 | A2 | 20040902 | WO 2004-US5191 | 20040220 |
| WO 2004074461 | A3 | 20050317 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

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|---|---|---|---|---|---|
| WO 2004074499 | A2 | 20040902 | WO 2004-US5244 | | 20040220 |
| WO 2004074499 | A3 | 20050127 | | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| EP 1597379 | A2 | 20051123 | EP 2004-713369 | | 20040220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| EP 1597380 | A2 | 20051123 | EP 2004-713372 | | 20040220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| EP 1597381 | A2 | 20051123 | EP 2004-713388 | | 20040220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| EP 1599595 | A2 | 20051130 | EP 2004-713412 | | 20040220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| EP 1599596 | A2 | 20051130 | EP 2004-713437 | | 20040220 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| US 2006040353 | A1 | 20060223 | US 2005-108088 | | 20050415 |
| US 2006024304 | A1 | 20060202 | US 2005-187196 | | 20050721 |
| US 2006029604 | A1 | 20060209 | US 2005-187229 | | 20050721 |
| US 2006034828 | A1 | 20060216 | US 2005-187066 | | 20050721 |
| US 2006034830 | A1 | 20060216 | US 2005-187113 | | 20050721 |
| US 2006078963 | A1 | 20060413 | US 2005-240432 | | 20050930 |
| US 2006148035 | A1 | 20060706 | US 2005-271235 | | 20051110 |
| PRIORITY APPLN. INFO.: | | | US 2000-214358P | P | 20000628 |
| | | | US 2000-215638P | P | 20000630 |
| | | | US 2001-279997P | P | 20010330 |
| | | | US 2001-892591 | A2 | 20010627 |
| | | | EP 2001-954606 | A3 | 20010627 |
| | | | US 2001-344169P | P | 20011227 |
| | | | WO 2002-US41510 | A2 | 20021224 |
| | | | US 2003-371877 | A2 | 20030220 |
| | | | US 2003-616082 | A | 20030708 |
| | | | US 2003-680963 | A | 20031007 |
| | | | US 2003-695243 | A | 20031027 |
| | | | WO 2004-US5128 | A | 20040220 |
| | | | WO 2004-US5131 | A | 20040220 |
| | | | WO 2004-US5132 | W | 20040220 |
| | | | WO 2004-US5191 | A | 20040220 |
| | | | WO 2004-US5244 | A | 20040220 |
| | | | US 2004-562424P | P | 20040415 |
| | | | US 2004-589926P | P | 20040721 |
| | | | US 2004-589979P | P | 20040721 |
| | | | US 2004-589981P | P | 20040721 |
| | | | US 2004-589988P | P | 20040721 |
| | | | US 2004-590011P | P | 20040721 |
| | | | US 2004-590051P | P | 20040721 |
| | | | US 2004-639657P | P | 20041223 |
| | | | US 2004-639698P | P | 20041223 |
| | | | US 2005-500240 | A2 | 20050323 |
| | | | US 2005-108088 | A2 | 20050415 |

AB The present invention relates to use of combinatorial DNA library of mammalian glycosylation enzyme genes for producing modified n-glycans in lower eukaryotes. The invention provides nucleic acid mols. and combinatorial libraries which can be used to successfully target and

express mammalian enzymic activities such as those involved in glycosylation to intracellular compartments in a eukaryotic host cell. Heterologous expression of a set of glycosyltransferases, sugar transporters and mannosidases in eukaryotic host cells enables oligosaccharide modification and the development of host-strains for the production of mammalian glycoproteins. The process provides an engineered host cell which can be used to express and target any desirable gene(s) involved in glycosylation. Host cells with modified oligosaccharides are created or selected. N-glycans made in the engineered host cells have a Man 5 GlcNAc 2 core structure which may then be modified further by heterologous expression of one or more enzymes, e.g., glycosyltransferases, sugar transporters and mannosidases, to yield human-like glycoproteins. With the primary goal of production of human therapeutic glycoproteins, this method may be adapted to engineer cell lines in which any desired glycosylation structure may be obtained.

L5 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Production of glycoproteins with modified glycosylation in Pichia pastoris
SO PCT Int. Appl., 172 pp.
CODEN: PIXXD2

ACCESSION NUMBER: 2004:20853 CAPLUS
DOCUMENT NUMBER: 140:88711
TITLE: Production of glycoproteins with modified glycosylation in Pichia pastoris
INVENTOR(S): Contreras, Roland; Callewaert, Nico L. M.; Geysens, Steven C. J.; Kaigorodov, Vladimir; Wouter, Vervecken
PATENT ASSIGNEE(S): Flanders Interuniversity Institute for Biotechnology, Belg.
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004003194 | A2 | 20040108 | WO 2003-EP6711 | 20030625 |
| WO 2004003194 | A3 | 20040422 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004018588 | A1 | 20040129 | US 2002-185475 | 20020626 |
| CA 2490268 | AA | 20040108 | CA 2003-2490268 | 20030625 |
| AU 2003238051 | A1 | 20040119 | AU 2003-238051 | 20030625 |
| EP 1516048 | A2 | 20050323 | EP 2003-735682 | 20030625 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006502705 | T2 | 20060126 | JP 2004-516676 | 20030625 |
| NO 2005000410 | A | 20050323 | NO 2005-410 | 20050125 |
| PRIORITY APPLN. INFO.: | | | US 2002-185475 A | 20020626 |
| | | | WO 2003-EP6711 W | 20030625 |

AB The present invention provides genetically engineered strains of methylotrophic yeast including Pichia and especially Pichia pastoris

capable of producing proteins with reduced or modified glycosylation. Methods of producing glycoproteins with reduced and/or modified glycosylation using such genetically engineered strains of Pichia are also provided. Vectors, which comprise coding sequences for α-1,2-mannosidase I, glucosidase II, GlcNAc-transferase I and mannosidase II or comprising OCH1 disrupting sequence, for transforming methylotrophic yeasts are contemplated by the present invention. Kit for providing the contemplated vectors are also included in this invention.

L5 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Methods for production of recombinant glycoproteins with mammalian-type carbohydrate structures and their use for production of immunoglobulins
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2

ACCESSION NUMBER: 2003:551280 CAPLUS
DOCUMENT NUMBER: 139:112733
TITLE: Methods for production of recombinant glycoproteins with mammalian-type carbohydrate structures and their use for production of immunoglobulins
INVENTOR(S): Wildt, Stefan; Miele, Robert Gordon; Nett, Juergen Hermann; Davidson, Robert C.
PATENT ASSIGNEE(S): Glycofi, Inc., USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 20
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2003056914 | A1 | 20030717 | WO 2002-US41510 | | 20021224 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2471551 | AA | 20030717 | CA 2002-2471551 | | 20021224 |
| AU 2002358296 | A1 | 20030724 | AU 2002-358296 | | 20021224 |
| EP 1467615 | A1 | 20041020 | EP 2002-792535 | | 20021224 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | | |
| JP 2005514021 | T2 | 20050519 | JP 2003-557288 | | 20021224 |
| US 2005170452 | A1 | 20050804 | US 2003-500240 | | 20021224 |
| US 2004230042 | A1 | 20041118 | US 2003-616082 | | 20030708 |
| US 2005208617 | A1 | 20050922 | US 2003-680963 | | 20031007 |
| US 2006040353 | A1 | 20060223 | US 2005-108088 | | 20050415 |
| US 2006024292 | A1 | 20060202 | US 2005-187065 | | 20050721 |
| US 2006029604 | A1 | 20060209 | US 2005-187229 | | 20050721 |
| US 2006034829 | A1 | 20060216 | US 2005-187079 | | 20050721 |
| US 2006034830 | A1 | 20060216 | US 2005-187113 | | 20050721 |
| PRIORITY APPLN. INFO.: | | | US 2001-344169P | P | 20011227 |
| | | | US 2000-214358P | P | 20000628 |
| | | | US 2000-215638P | P | 20000630 |
| | | | US 2001-279997P | P | 20010330 |

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|---|---|---|
| US 2001-892591 | A2 | 20010627 |
| WO 2002-US41510 | W | 20021224 |
| US 2003-371877 | A2 | 20030220 |
| US 2004-562424P | P | 20040415 |
| US 2004-589913P | P | 20040721 |
| US 2004-589937P | P | 20040721 |
| US 2004-590011P | P | 20040721 |
| US 2004-590030P | P | 20040721 |
| US 2004-590051P | P | 20040721 |
| US 2004-590052P | P | 20040721 |
| US 2004-639657P | P | 20041223 |
| US 2004-639698P | P | 20041223 |
| US 2005-500240 | A2 | 20050323 |
| US 2005-108088 | A2 | 20050415 |

AB The present invention relates to host cells having modified lipid-linked oligosaccharides which may be modified further by heterologous expression of a set of glycosyltransferases, sugar transporters and mannosidases to become host-strains for the production of mammalian, e.g., human therapeutic glycoproteins. The process provides an engineered host cell which can be used to express and target any desirable gene(s) involved in glycosylation. Host cells with modified lipid-linked oligosaccharides are created or selected. N-glycans made in the engineered host cells have a GlcNAcMan3GlcNAc2 core structure which may then be modified further by heterologous expression of one or more enzymes, e.g., glycosyltransferases, sugar transporters and mannosidases, to yield human-like glycoproteins. For the production of therapeutic proteins, this method may be adapted to engineer cell lines in which any desired glycosylation structure may be obtained. The invention specifically claims use of nucleic acid sequences for gene ALG3 from Pichia pastoris. The ALG3 gene encodes the enzyme which transfers a mannose residue to the Man5-GlcNac2-PP-Dol precursor. The invention also claims use of genetically engineered host cells for recombinant production of Igs. In examples of the invention, a Pichia pastoris strain with deletions of genes alg3 and och1 was constructed. This strain was transformed with the Kringle 3 domain of human plasminogen as a glycosylation substrate. Mass spectrometric anal. of N-glycans isolated from the kringle 3 glycoproteins showed GlcNAcMan3GlcNAc2 and GlcNAcMan4GlcNAc2 structures which could be further modified in vitro. Addition of N-acetylglucosamine to GlcNAcMan3GlcNAc2 by N-acetylglucosaminyltransferases II and III yields a "bisected" N-glycan, GlcNAc3Man3GlcNAc2, which has been implicated in greater antibody-dependent cellular cytotoxicity. Methods of the invention can be used to engineer a yeast strain capable of producing glycoproteins with bisected N-glycans and expressing Ig mols. with bisected N-glycans attached to asparagine residue 297 in the CH2 portion.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN

TI Use of combinatorial genetic libraries to humanize N-linked glycosylation in the yeast Pichia pastoris

SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(9), 5022-5027
CODEN: PNASA6; ISSN: 0027-8424

ACCESSION NUMBER: 2003:368101 CAPLUS

DOCUMENT NUMBER: 139:95996

TITLE: Use of combinatorial genetic libraries to humanize N-linked glycosylation in the yeast Pichia pastoris

AUTHOR(S): Choi, Byung-Kwon; Bobrowicz, Piotr; Davidson, Robert C.; Hamilton, Stephen R.; Kung, David H.; Li, Huijuan; Miele, Robert G.; Nett, Juergen H.; Wildt, Stefan; Gerngross, Tillman U.

CORPORATE SOURCE: Thayer School of Engineering, Dartmouth College, Hanover, NH, 03755, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2003), 100(9), 5022-5027
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The secretory pathway of Pichia pastoris was genetically re-engineered to perform sequential glycosylation reactions that mimic early processing of N-glycans in humans and other higher mammals. After eliminating nonhuman glycosylation by deleting the initiating α-1,6-mannosyltransferase gene from P. pastoris, several combinatorial genetic libraries were constructed to localize active α-1,2-mannosidase and human β-1,2-N- acetylglucosaminyltransferase I (GnTI) in the secretory pathway. First, >32 N-terminal leader sequences of fungal type II membrane proteins were cloned to generate a leader library. Two addnl. libraries encoding catalytic domains of α-1,2-mannosidases and GnTI from mammals, insects, amphibians, worms, and fungi were cloned to generate catalytic domain libraries. In-frame fusions of the resp. leader and catalytic domain libraries resulted in several hundred chimeric fusions of fungal targeting domains and catalytic domains. Although the majority of strains transformed with the mannosidase/leader library displayed only modest in vivo [i.e., low levels of mannose (Man)5-(GlcNAc)2] activity, we were able to isolate several yeast strains that produce almost homogenous N-glycans of the (Man)5-(GlcNAc)2 type. Transformation of these strains with a UDP-GlcNAc transporter and screening of a GnTI leader fusion library allowed for the isolation of strains that produce GlcNAc-(Man)5-(GlcNAc)2 in high yield. Recombinant expression of a human reporter protein in these engineered strains led to the formation of a glycoprotein with GlcNAc-(Man)5-(GlcNAc)2 as the primary N-glycan. Here we report a yeast able to synthesize hybrid glycans in high yield and open the door for engineering yeast to perform complex human-like glycosylation.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Modification of the N-glycosylation pathway of lower eukaryotes to a mammalian type
SO Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), BIOT-030 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69DSA4
ACCESSION NUMBER: 2003:179025 CAPLUS
TITLE: Modification of the N-glycosylation pathway of lower eukaryotes to a mammalian type
AUTHOR(S): Contreras, Roland H.; Vervecken, Wouter; Callewaert, Nico; Geysens, Steven; Kaigorodov, Vladimir
CORPORATE SOURCE: Molecular Biology, Ghent University and VIB, B-9000 Gent, Belg.
SOURCE: Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), BIOT-030. American Chemical Society: Washington, D. C.
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AB Lower eukaryotes only synthesize N-glycans of the high-mannose type, whereas human glycoproteins have a very divers, complex type of N-glycans. Redirection of the fungal pathway, even to a simple hybrid or complex mammalian type requires several genetic

interventions such as gene knock-outs and heterologous expression of mammalian glycosyl transferases. Furthermore, addnl. in vitro enzymic manipulations may be required. In general, it seems that humanising N-glycans from filamentous fungi is an easier task than modifying yeast protein linked carbohydrates because the long alfa-1,6-arm apparently is absent. The problem is reduced to importing an efficient alfa-1,2-mannosidase and addition of complex sugar glycosyl transferases. We started a strategy to humanise the N-glycosylation pathway in the filamentous fungus Aspergillus niger NW195. In a first step a HDEL tagged a-1,2-mannosidase from Trichoderma reesei was introduced. The over expression of this enzyme lead to the conversion of the majority of the N-glycans to Man5GlcNAc2 (ca. 80%). In a second step the over expression of human N&64979;acetylglucosaminyltransferase I lead to the detection of GlcNAcMan5GlcNAc2 structures. The percentage conversion of Man5GlcNAc2 to GlcNAcMan5GlcNAc2 was inversely related to the amount of protein that was synthesized, ranging from ca. 40% to merely all. Yeasts, like S. cerevisiae and P. pastoris, have an extra, long alfa-1,6-arm that is mannose and P-mannose rich. Eliminating this structure causes, at least in S. cerevisiae, a weak growth and temperature sensitive phenotype. Different procedures have been followed to knock out the OCH1 gene. Expression of alfa-1,2-mannosidase has also been obtained in combination with OCH1 knock out, resulting in very high yileds of Man5GlcNAc2 N-linked structures. Furthermore, phosphodiester linked mannoses are, in general, unwanted in mammalian therapeutic situations. Knock out of phosphomannosyltransferases is required to eliminate these structures from yeast and fungal protein linked sugars. Cloning of the P. pastoris homologues of S. cerevisiae MNN4 and MNN6 genes is not an easy task. Ultimately, the terminal sialic acid should be added using in vitro procedures.

L5 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
TI Engineering of intracellular sialylation pathways for sialylated glycoprotein production
SO PCT Int. Appl., 145 pp.
CODEN: PIXXD2

ACCESSION NUMBER: 2000:628243 CAPLUS
DOCUMENT NUMBER: 133:233546
TITLE: Engineering of intracellular sialylation pathways for sialylated glycoprotein production
INVENTOR(S): Betenbaugh, Michael J.; Lawrence, Shawn; Lee, Yuan C.; Jarvis, Don; Coleman, Timothy A.
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA; Johns Hopkins University; University of Wyoming
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2000052135 | A3 | 20040108 | | |

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| CA 2363297 | AA | 20000908 | CA 2000-2363297 | | 20000301 |
| AU 2000035083 | A5 | 20000921 | AU 2000-35083 | | 20000301 |
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| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY | | | | | |
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AB Methods for manipulating carbohydrate processing pathways in cells of interest are provided. Methods are directed at manipulating multiple pathways involved with the sialylation reaction by using recombinant DNA technol. and substrate feeding approaches to enable the production of sialylated glycoproteins in cells of interest. These carbohydrate engineering efforts encompass the implementation of new carbohydrate bioassays, the examination of a selection of insect cell lines and the use of bioinformatics to identify gene sequences for critical processing enzymes. The compns. comprise cells of interest producing sialylated glycoproteins. The methods and compns. are useful for heterologous expression of glycoproteins. Thus, the cDNA for a human sialic acid 9-phosphate synthetase which produces phosphorylated KDN and Neu5Ac from ManNAc-6-P and Man-6-P was cloned and sequenced. Sf9 cells infected with a baculovirus encoding this enzymes produced enhanced levels of sialic acids when the culture medium was supplemented with ManNAc.

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| L1 | 150064 | S | GLYCOPROTEIN |
| L2 | 881 | S | L1 AND YEAST AND HUMAN |
| L3 | 14 | S | GNT1 |
| L4 | 1667 | S | ACETYLGLUCOSAMINYLTRANSFERASE |
| L5 | 27 | S | L2 AND L4 |
| L6 | 27 | DUP REM | L5 (0 DUPLICATES REMOVED) |